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Ambient Water Quality Criteria 2,4-Dichlorophenol

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2,4-DICHLOROPHENOL

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
U.S. Environmental Protection Agency
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CRITERION DOCUMENT
2,4-DICHLOROPHENOL

CRITERIA

Aquatic Life

For 2,4-dichlorophenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.4 µg/l as a 24-hour average and the concentration should not exceed 110 µg/l at any time.

For saltwater aquatic life, no criterion for 2,4-dichlorophenol can be derived using the Guidelines, and there are insufficient data to estimate a criterion using other procedures.

Human Health

For the prevention of adverse effects due to the organoleptic properties of 2,4-dichlorophenol in water, the criterion is 0.5 µg/l.

BIBLIOGRAPHIC INFORMATION

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Ambient Water Quality Criteria: 2,4-Dichlorophenol.

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Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for 2,4-dichlorophenol. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itse, ...

KEYWORDS: *Water quality, *Toxicology, *Water pollution effects(Humans), *Water pollution effects(Animals), *Toxic substances, *Phenol/dichloro, *DCP 2-4 herbicide, *Water pollution effects(Plants).

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Introduction

2,4-dichlorophenol (2,4-DCP) is a commercially produced substituted phenol used entirely in the manufacture of industrial and agricultural products. As an intermediate in the chemical industry, 2,4-DCP is utilized principally as the feedstock for the manufacture of the herbicide, 2,4-dichlorophenoxyacetic acid (2,4-D), 2,4-D derivatives (germicides, soil sterilants, etc.) and certain methyl compounds used in mothproofing, antiseptics and seed disinfectants. 2,4-DCP is also reacted with benzene sulfonyl chloride to produce miticides or further chlorinated to pentachlorophenol, a wood preservative (U.S. EPA, 1975).

2,4-dichlorophenol is a colorless, crystalline solid having the empirical formula $C_6H_4Cl_2O$, a molecular weight of 163.0 (Weast, 1975), a density of 1.383 at 60 degrees F/25 degrees C and a vapor pressure of 1.0 mm Hg at 53.0 degrees C (Sax, 1975). The melting point of 2,4-DCP is 45 degrees C and the boiling point is 210 degrees C at 760 mm Hg (Aly and Faust, 1965; Weast, 1975).

2,4-DCP is slightly soluble in water at neutral pH and dissolves readily in ethanol and benzene (Kirk and Othmer, 1964). 2,4-DCP behaves as a weak acid and is highly soluble in alkaline solutions, since it readily forms the corresponding alkaline salt. The dissociation constant (pKa) for 2,4-DCP has been reported to be 7.48 (Pearch and Simpkins, 1968). Unlike the monochlorophenols, 2,4-DCP is not volatile from aqueous alkaline solutions (Kirk and Othmer, 1964).

2,4-DCP is readily prepared without benefit of a catalyst using gaseous chlorine and molten phenol at 80 to 100 degrees C. Synthesis is also attainable through the chlorination of the monochlorophenols (Kirk and Othmer, 1972).

It has been demonstrated that phenol is quite reactive to chlorine in dilute aqueous solutions over a wide pH range (Carlson and Caple, 1975; Middaugh and Davis, 1976).

Although 2,4-DCP presently has no direct commercial application, its use as an important chemical intermediate, its synthesis from dilute aqueous solutions, and its identification as a metabolic intermediate and degradation product of various commercial products by plants (Kirk and Othmer, 1972), microorganisms (Kearney and Kaufman, 1972; Steenson and Walker, 1957; Bell, 1957, 1960; Evans and Smith, 1954; Fernley and Evans, 1959; Loos, et al. 1967a, b; Loos, 1969) and sunlight (Aly and Faust, 1964; Crosby and Tutass, 1966; Mitchell, 1961) has been well established. This clearly indicates its importance as a potential point source and non-point source water contaminant.

Little information is available on the 2,4-DCP levels present in industrial or municipal effluents, natural waters, or drinking water. A report by Sidwell (1971) found 2,4-DCP levels in industrial plant effluents ranging from 11.4 to 73.6 mg/l and has estimated a resulting drinking water level of 1.25 mg/l. Additionally, oxidative degradation of 2,4-DCP in natural lake waters under laboratory conditions has also been reported (Aly and Faust, 1964).

Numerous studies on the microbial degradation of 2,4-DCP have been conducted, revealing degradation to yield succinic acid (Alexander and Aleem, 1961; Macrae, et al. 1963; Paris and Lewis, 1973; Fernley and Evans, 1959; Bell, 1957, 1960; Bollag, et al. 1968a; Macrae and Alexander, 1965; Chu and Kirsch, 1972; Ingols, et al. 1966; Bollag, et al. 1968b; Chapman, 1972; Duxbury, et al. 1970; Loos, et al. 1967b; Tiedje, et al. 1969).

Few data exist regarding the persistence of 2,4-DCP in the environment. 2,4-DCP is slightly soluble in water while its alkaline salts are readily soluble in aqueous solutions. Its low vapor pressure and non-volatility from alkaline solutions would cause it to be only slowly removed from surface water via volatilization. Studies have indicated low sorption of 2,4-DCP from natural surface waters by various clays (Aly and Faust, 1964).

Little or no information on the bioconcentration, metabolism, or excretion of 2,4-DCP appears to exist. However, an octanol/water partition coefficient of 1,200 has been reported.

Although a paucity of aquatic toxicity data exists, 2,4-DCP appears to be less toxic than the higher chlorinated phenols. 2,4-DCP's toxicity to certan microorganisms and plant life has been demonstrated and its tumor promoting potential in mice (Boutwell and Bosch, 1959) has been reported. In addition, it has been demonstrated that 2,4-DCP can produce objectionable odors when present in water at extremely low

levels (Burttschell, et al. 1959). These findings, in conjunction with potential 2,4-DCP pollution by waste sources from commercial processes or the inadvertent production of 2,4-DCP due to chlorination of waters containing phenol, lead to the conclusion that 2,4-DCP represents a potential threat to aquatic and terrestrial life, including man.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Although 2,4-dichlorophenol has been used as a chemical intermediate in the manufacture of herbicides, germicides, temporary soil sterilants, plant growth regulators, moth proofing agents, seed disinfectants, miticides, and wood preservatives for years, few acute toxicity data and no chronic toxicity data are available for freshwater aquatic organisms. Flavor-impairment studies with 2,4-dichlorophenol showed that flesh tainting in fish occurred at much lower concentrations than either acute toxicity effects on fish and invertebrate species or toxic effects on plants. For this reason, flavor-impairment information was used in deriving a criterion for freshwater aquatic organisms for 2,4-dichlorophenol.

Acute Toxicity

Only two acute values for 2,4-dichlorophenol toxicity on freshwater fish were available in the literature (Table 1) and only one of these tests was conducted using flow-through conditions and measured concentrations. Phipps, et al.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] and the Methodology Document in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

(manuscript) calculated a 96-hour LC50 of 8,230 µg/l for fathead minnows. This is almost 8 times higher than the adjusted 96-hour LC50 of 1,104 µg/l for bluegills determined under static test conditions (U.S. EPA, 1978). The sensitivity factor of 3.9 yields a Final Fish Acute Value that is more likely to protect 95 percent of freshwater fish species than the lowest value from a flow-through test with measured concentrations. The Final Fish Acute Value is 770 µg/l which is only slightly lower than the adjusted 96-hour LC50 for the most sensitive species tested and suggests a reasonable fit of the data to the procedures in the Guidelines.

The data base for invertebrate species (Table 2) consists of two static tests on a single cladoceran species. The adjusted 48-hour LC50 values determined for Daphnia magna by Kopperman, et al. (1974) and U.S. EPA (1978) were 2,211 µg/l and 2,202 µg/l, respectively. Since not enough data are available to make any decision on the relative sensitivity of invertebrate species, and since no flow-through tests with measured concentrations are available, the Guideline's procedures are used to derive the Final Invertebrate Acute Value of 110 µg/l. This value is lower than the Final Fish Acute Value of 770 µg/l (Table 1) and becomes the Final Acute Value for freshwater aquatic life.

The 96-hour LC50 values for chlorinated phenols and bluegills (U.S. EPA, 1978) in this and other criterion documents are directly related to the degree of chlorination. These values decrease from 6,590 µg/l for 2-chlorophenol and 3,830

µg/l for 4-chlorophenol to 60 and 70 µg/l for pentachlorophenol. These data and those for 2,4-dichlorophenol and other intermediate chlorinated phenols can be correlated with the n-octanol/water partition coefficient with a correlation coefficient of 0.95. Data for other species do not correlate as well.

Chronic Toxicity

There are no data available on the chronic toxicity of 2,4-dichlorophenol to freshwater aquatic life.

Plant Effects

The toxicity of 2,4-dichlorophenol to freshwater aquatic plants does not appear important in the derivation of the criterion since deleterious effects on plants (Table 3) occurred only at much higher concentrations than those which produced acute toxic effects on fish and invertebrate species. However, the knowledge that 2,4-dichlorophenol is not highly toxic to plants is important because 2,4-dichlorophenol is used in producing the commonly used herbicide, 2,4-D (2,4-dichlorophenoxyacetic acid). Some observed toxic effects of 2,4-dichlorophenol on plants were the complete destruction of chlorophyll in Chlorella pyrenoidosa at 100,000 µg/l (Huang and Gloyna, 1968) and a 50 percent reduction in chlorophyll in Lemna minor at 58,320 µg/l (Blackman, et al. 1955). The Final Plant Value is 50,000 µg/l based on data of Huang and Gloyna (1968) who determined that there was a 56.4 percent reduction of photosynthetic oxygen production in Chlorella pyrenoidosa after 120 minutes.

Residues

No measured steady-state bioconcentration factor (BCF) is available for 2,4-dichlorophenol. A BCF can be estimated using the octanol/water partition coefficient of 1,200. This coefficient is used to derive an estimated BCF of 130 for aquatic organisms that contain about 8 percent lipids. If it is known that the diet of the wildlife of concern contains a significantly different lipid content, an appropriate adjustment in the estimated BCF should be made.

Miscellaneous

Except for the studies dealing with flavor impairment in fish, Table 4 contains no data which would appear to alter the derivation of the criterion for 2,4-dichlorophenol. Flavor-impairment studies (Shumway and Palensky, 1973) showed that concentrations of 2,4-dichlorophenol, when exceeded, cause tainting to occur at concentrations ranging from 0.4 µg/l to 14.0 µg/l for the various species of fish tested (Table 4). Based on the available data for 2,4-dichlorophenol, flavor impairment in fish occurs at lower concentrations than other effects used to express toxicity and should be used in setting a criterion. Since the purpose of the Guidelines is to set water quality criteria which protect both the presence and uses of aquatic life, a criterion of 0.4 µg/l is necessary to protect the quality of the freshwater fishery.

CRITERION FORMULATION

Freshwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 770 µg/l

Final Invertebrate Acute Value = 110 µg/l

Final Acute Value = 110 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 50,000 µg/l

Residue Limited Toxicant Concentration = not available

Final Chronic Value = 0.4 µg/l for tainting

0.44 x Final Acute Value = 48 µg/l

The maximum concentration of 2,4-dichlorophenol is the Final Acute Value of 110 µg/l and the 24-hour average concentration is the Final Chronic Value of 0.4 µg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For 2,4-dichlorophenol the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.4 µg/l as a 24-hour average and the concentration should not exceed 110 µg/l at any time.

Table 1. Freshwater fish acute values for 2,4-dichlorophenol

Organism	Bioassay Method*	Test Conc. **	Time (hrs.)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Fathead minnow (juvenile), Pimephales promelas	FT	M	96	8,230	8,230	Phipps, et al. Manuscript
Bluegill, Lepomis macrochirus	S	U	96	2,020	1,104	U.S. EPA, 1978

* S = static, FT = flow-through

** U = unmeasured, M = measured

Geometric mean of adjusted values = 3,014 µg/l $\quad \frac{3,014}{3.9} = 770$ µg/l

Lowest value from a flow-through test with measured concentrations = 8,230 µg/l

Table 2. Freshwater invertebrate acute values for 2,4-dichlorophenol

Organism	Bioassay Method *	Test Conc.**	Time (hrs.)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Cladoceran, Daphnia magna	S	U	48	2,610	2,211	Kopperman, et al. 1974
Cladoceran, Daphnia magna	S	U	48	2,600	2,202	U.S. EPA, 1978

* S = static

** U = unmeasured

Geometric mean of adjusted values = 2,206 µg/l $\frac{2,206}{21}$ = 110 µg/l

Table 3. Freshwater plant effects for 2,4-dichlorophenol

Organism	Effect	Concentration (ug/l)	Reference
Alga, *Chlorella pyrenoidosa*	Complete destruction of chlorophyll	100,000	Huang & Gloyna, 1968
Alga, *Chlorella pyrenoidosa*	56.4% reduction of photosynthetic oxygen production	50,000	Huang & Gloyna, 1968
Duckweed, *Lemna minor*	50% reduction in chlorophyll	58,320	Blackman, et al. 1955

Lowest plant value = 50,000 ug/l

Table 4. Other freshwater data for 2,4-dichlorophenol

Organism	Test Duration	Effect	Result (ug/l)	Reference
Lymnaeid snails, Pseudosuccinea columella Fossaria cubensis	24 hrs	100% mortality	10,000	Batte & Swanson, 1952
Crayfish, Orconectes propinquus Orconectes immunis Cambarus robustus	48 hrs	100% mortality	10,000	Telford, 1974
Crayfish, Orconectes propinquus Orconectes immunis Cambarus robustus	1 wk	100% mortality	5,000	Telford, 1974
Crayfish, Orconectes propinquus Orconectes immunis Cambarus robustus	10 days	14% mortality	1,000	Telford, 1974
Crayfish, Orconectes propinquus Orconectes immunis Cambarus robustus	10 days	Increased blood glucose levels	1,000	Telford, 1974
Rainbow trout, Salmo gairdneri	48 hrs	ETC*	1	Shumway & Palensky, 1973
Fathead minnow (juvenile), Pimephales promelas	192 hrs	LC50	6,500	Phipps, et al. Manuscript
Bluegill, Lepomis macrochirus	48 hrs	ETC*	14	Shumway & Palensky, 1973
Largemouth bass, Micropterus salmoides	48 hrs	ETC*	0.4	Shumway & Palensky, 1973

* ETC = the highest estimated concentration of material that will not impair the flavor of the flesh of exposed fish.

SALTWATER ORGANISMS

Introduction

The only data on the effects of 2,4-dichlorophenol on saltwater organisms is an acute exposure of the mountain bass, a species endemic to Hawaii, in which a moderate reaction was observed at a concentration of 20,000 ug/l (Hiatt, et al. 1953).

Residues

No measured steady-state bioconcentration factor (BCF) is available for 2,4-dichlorophenol. A BCF can be estimated using the octanol/water partition coefficient of 1,200. This coefficient is used to derive an estimated BCF of 130 for aquatic organisms that contain about 8 percent lipids. If it is known that the diet of the wildlife of concern contains a significantly different lipid content, an appropriate adjustment in the estimated BCF should be made.

CRITERION FORMULATION

Saltwater - Aquatic Life

No saltwater criterion can be derived for 2,4-dichlorophenol using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available, and there are insufficient data to estimate a criterion using other procedures.

Table 5. Other marine data for 2,4-dichlorophenol (Hiatt, et al. 1953)

Organism	Test Duration	Effect	Result µg/l
Mountain bass[1], *Kuhlia sandvicensis*	Acute response	Moderate reaction	20,000

[1]Endemic to Hawaii

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Mammalian Toxicology and Human Health Effects

EXPOSURE

Ingestion from Water

Absorption of 2,4-DCP by biological tissues may occur upon exposure to 2,4-DCP either dissolved in water or associated with suspended matter or sediments in water. Chlorophenols such as 2,4-DCP are weak acids that become increasingly ionized under alkaline conditions; they are mainly non-ionized at physiological pH. These properties together with the lipophilic nature of chlorophenols (including 2,4-DCP) make it likely that chlorophenols would be absorbed from the gastrointestinal tract.

Sources of 2,4-DCP in water may be diffuse (e.g., agricultural runoff) or localized (e.g., point source pollution from manufacturing waste discharges). Sidwell (1971) verified the presence of 2,4-DCP in 2,4-D manufacturing wastes. Over a 3-month period, total chlorophenol content ranged from 68 mg/l of waste to a high of 125 mg/l, with 2,4-DCP content ranging as high as 89 percent of the total. Details of these findings are presented in Table 2.

If certain assumptions are made, the data of Sidwell (1971) can be used to estimate human exposure to 2,4-DCP from drinking water obtained below a point source of this type. Assuming (1) an effluent with a 2,4-DCP concentration of 125 mg/l in water containing 100,000 mg/l of total solids (Table 2); (2) dilution in the watercourse occurring to

TABLE 2

Industrial Plant Effluent Content of Chlorophenols[a]

Date Sampled	25 Jan	3 Mar	21 Apr	28 May	27 Aug
Total Solids (mg/L)	6960	40,100	76,320	104,860	11,000
Temperature (°C)	12	18	21	28.5	24
pH	7.5	7.6	7.4	7.4	7.0
Chlorophenols (mg/L)	68	118	125	112	74
Phenol Type (%)[b]					
Phenol-	3.4	6.2	1.7	24.8	trace
2-chloro-	2.9	6.1	trace	trace	trace
2,4-dichloro-	73.6	17.9	20.0	11.4	89.0
2,6-dichloro-	9.9	41.7	38.8	30.5	3.0
2,5-dichloro-	trace	6.2	1.7	trace	1.8
4-chloro-	2.5	12.1	18.3	20.0	2.8
2,4,6-trichloro-	2.8	9.9	19.5	13.3	3.4
2,4,5-trichloro-	4.7	trace	trace	trace	trace

[a]Modified from Sidwell (1971)

[b]Percent of total phenols present

the point where an acceptable freshwater total solids concentration of 1,000 mg/l is reached; and (3) non-removal of 2,4-DCP by water treatment, drinking water will contain an estimated 1.25 mg/l of 2,4-DCP. If the daily water intake of a 70 kg person is assumed to be 2 liters, this would result in a daily dosage of 0.036 mg/kg body weight/day. It should be emphasized that this dosage is a worst case exposure level that would probably occur only in drinking water obtained below a 2,4-DCP-contaminated point source discharge.

Large amounts of 2,4-D released into the environment have been reported to cause 2,4-DCP contamination of groundwater. At Rocky Mountain Arsenal, phytotoxicity characteristic of 2,4-D exposure was noted at distances up to 5.6 km from 2,4-D waste storage lagoons (Walker, 1961).

If diffuse or point source contamination of waters with 2,4-DCP is in fact occurring, the dissipation of this compound in aquatic environments becomes an important consideration. The major avenues of 2,4-DCP dissipation that have been studied are microbial degradation and photodecomposition. Aly and Faust (1964) examined the dissipation of 2,4-DCP from natural lake waters at a buffered pH of 7. In aerated lake waters, with initial 2,4-DCP concentrations of 100, 500, and 1,000 µg/l, the percentages of 2,4-DCP remaining at 9 days were 0, 0.34, and 46 respectively. By contrast, initial concentrations of 100, 500, and 1,000 µg/l in unaerated and unbuffered waters resulted in percentages

of 40, 51.6, and 56 at 17 days. Aly and Faust concluded that the persistence of chlorophenol would tend to increase at lower pH and under anaerobic conditions that might result from the decomposition of excessive organic matter.

Ingols, et al. (1966) studied the degradation of various chlorophenols by activated sewage sludge and concluded that 2,4-DCP was degraded more rapidly by activated systems with previous exposure to chlorophenols than by those with no previous exposure to chlorophenols. When activated sludge was exposed to 2,4-DCP at levels of 100 mg/l of sludge, 75 percent of the chemical disappeared in 2 days and essentially 100 percent was gone in 5 days. Hemmett (1972) showed that microorganisms acclimated to the herbicide 2,4-D could degrade 2,4-DCP without a lag period, implying similar biological pathways for the two compounds.

When 2,4-DCP was subjected to aeration basin treatment, the initial concentration of 64 mg/l dropped to an undetectable level within 5 days (Sidwell, 1971), which was more rapid than the rate of degradation observed for 2,4-DCP in distilled water. When an aerated lagoon alone was used, removal of all chlorophenols varied from 55 to 89 percent, whereas overall removal using both lagoon and stabilization ponds ranged from 87 to 94 percent. Thus, heavy loads of chlorophenol contamination may be largely dissipated by attention to effluent waste management.

Dissipation of dichlorophenols also occurs through photodecomposition in aqueous solutions. Aly and Faust (1964) demonstrated that (1) 2,4-DCP was decomposed by ultra-

violet light, and (2) the rate of photolysis in distilled water decreased as pH decreased. Degradation of 50 percent of 2,4-DCP by ultraviolet light was accomplished in 2 minutes at pH 9.0, in 5 minutes at pH 7.0, and in 34 minutes at pH 4.0. The studies of Aly and Faust were conducted with light of wavelength 253.7 nm, which is slightly shorter than the natural ultraviolet radiation wavelength range of 292 to 400 nm.

The riboflavin-sensitized dimerization of DCP to tetrachlorodiphenyl ethers, tetrachlorodihydroxy-biphenyls, and other products was reported by Plimmer and Klingebiel (1971). Chlorinated dibenzo-p-dioxins, which could have resulted from ring closure of these tetrachlorodiphenyl ethers, were not detected in the products of photolysis. The authors speculated that failure to detect chlorinated dibenzo-p-dioxins may have been due to the rapid photolytic breakdown of those dioxins. Rapid photolysis of chlorinated dibenzo-p-dioxins was confirmed by Crosby, et al. (1971).

2,4-DCP has been reported as a photolytic product of the herbicides 2,4-D and nitrofen (2,4-dichlorophenyl p-nitrophenyl ether) in aqueous suspension under sunlight or simulated sunlight, as noted by several investigators, including Aly and Faust (1964), Zepp, et al. (1975), and Nakagawa and Crosby (1974, a,b). Crosby and Tutass (1966) irradiated 2,4-D with artificial light (254 nm) and natural sunlight and observed that under both conditions 2,4-dichlorophenol was formed as a photolytic product of 2,4-D and was further degraded to 4-chlorocatechol. 2,4-DCP was photolabile with 50 percent being lost in 5 minutes at pH 7.0.

Microbial decomposition of 2,4-DCP in soils and aquatic environments has been extensively studied. Alexander and Aleem (1961) found that when 80 µg 2,4-DCP/ml medium was incubated in the presence of Dunkirk silt loam and Mardin silt loam, 2,4-DCP was not detectable after 9 and 5 days respectively. When these soil preparations were treated with sodium azide, no disappearance of 2,4-DCP was noted, supporting the role of microbiological processes in the degradation. Loos, et al. (1967 a,b) found that extracts of Arthrobacter sp. contained enzymes capable of dehalogenating 2,4-dichlorophenol. Degradation was rapid with 100 percent chloride release from 2,4-DCP occurring after 4 hours of incubation. The cells responsible for the dehalogenating process were active when cultured on the herbicides 2,4-D or 2-methyl-4-chlorophenoxyacetate (MCPA). Kearney, et al. (1972) found no tetrachlorodibenzo-p-dioxin in soils treated with up to 1,000 µg/g of 2,4-DCP. Sharpee (1973) measured 2,4-DCP in the soil as a consequence of 2,4-D application and found that 2,4-DCP did appear in soil treated with 2,4-D, but it did not persist as long as the 2,4-D.

As indicated earlier, the principal source of 2,4-DCP in soils is expected to be the herbicide 2,4-D. The various intermediates (including 2,4-DCP) in the microbial metabolism of 2,4-D have been characterized by several investigators (Spokes and Walker, 1974; Loos, et al., 1967 a,b; Bollag, et al., 1968; Evans, et al., 1971; Paris and Lewis, 1973; Ingols, et al., 1966; Alexander and Aleem, 1961). Kearney and Kaufman (1972) have shown that the organisms capable

of degrading 2,4-D to 2,4-DCP continue the degradation process to catechol intermediates and finally to succinic acid. Thus, the pesticide 2,4-D is eventually biodegraded to an ecologically acceptable product, succinic acid.

Recently, attention has focused on a potential chlorophenol source of a more ubiquitous nature than pesticide applications. Both municipal and industrial wastewater are often subjected to chlorination to achieve disinfection and deodorization (Barnhart and Campbell, 1972). One result of chlorination is the reaction of chlorine with phenol to produce chlorophenols, some of which are a source of obnoxious odors and/or taste (Barnhart and Campbell, 1972; Burtschell, et al., 1959; Hoak, 1957).

Phenol was observed to be quite reactive with chlorine in dilute aqueous solutions. This high reactivity of phenol is attributed to the ring-activating electron-releasing properties of the -OH functional group (Barnhart and Campbell, 1972; Morris, 1978). Halogen substitution is preferentially favored in the ortho- and para- positions (Burtschell, et al., 1959).

Chlorination of phenols results in a stepwise substitution of the 2, 4, and 6 positions of the aromatic ring. Barnhart and Campbell (1972) felt that it was probable that chlorination resulted in a complex mixture of chlorophenols. Burtschell, et al. (1959) chlorinated 1 liter of approximately 20 µg/ml of a phenol solution containing 2 g/l sodium bicarbonate with 40 mg chlorine, and isolated 2,4-DCP as one of three major chlorophenols. Relative chlorophenol

content determined in this study was as follows:

Component	Percent of Product
Phenol	1-2
2-Chlorophenol	2-5
4-Chlorophenol	2-5
2,4-Dichlorophenol	20
2,6-Dichlorophenol	25
2,4,6-Trichlorophenol	40-50

(Absolute amounts of chlorophenols were not reported.)

Lee and Morris (1962) verified the stepwise chlorination of phenol to chlorophenolic compounds. Furthermore, they determined that the reaction rate and yield of 2,4-DCP is quite pH dependent, with a decrease in generation time and an increase in yield for 2,4-DCP as pH increases from 7 to 9. The reactions occurred at initial chlorine concentrations of 1 µg/g and phenol concentrations of 50 ng/g.

Jolley (1973) indicated that development of chlorinated organics, including chlorinated phenols, is retarded in solutions with high ammonia concentrations. In a later study, Jolley, et al. (1978) examined the chlorination of sewage waters under conditions simulating those used for disinfection of sewage effluents and/or antifoulant treatment of cooling waters of electric power generating plants. Over 50 chloro-organic constituents were separated in each analysis of concentrated sewage effluent chlorinated in the laboratory with 2.5 to 6 mg/l concentrations of chlorine. Similar studies were also done on two bodies of lake water, each receiving effluent from a coal-fired, electric-power generating plant. In contrast to their earlier studies, Jolley, et al. (1978) found mono-chlorophenols at ng/g levels in the three systems examined but no dichlorophenols.

Glaze, et al. (1978) identified trichlorophenols but no dichlorophenols in superchlorinated municipal wastewaters. Thus, in contrast to laboratory demonstrations of DCP formation, recent work under conditions simulating the natural environment has not established that 2,4-DCP is a significant product resulting from chlorination of phenol-containing waters.

Ingestion from Food

Any 2,4-DCP contamination of food products (non-aquatic) would probably result from use of the herbicide 2,4-D. As stated earlier, 2,4-DCP is a contaminant of 2,4-D as well as an intermediate compound in the biological degradation of 2,4-D.

Absorption of 2,4-DCP has been reported for some plant species (Isensee and Jones, 1971). Total DCP content in oat and soybean plants increased for approximately 3 weeks when the soil contained a DCP concentration of 70 µg/g. As these plants grew, the total tissue content of DCP remained relatively constant but decreased as the plants matured. At time of harvest, oats contained 0.01 µg of DCP per gram of plant tissue and soybeans contained 0.02 µg/g. The 2,4-DCP did not seem to concentrate in the plant seeds. DCP was not detected in the grain of these oat plants, and the soybean seeds contained only 1 to 2 percent of the total plant DCP. No evidence was found of DCP translocation in soybeans after foliar application.

2,4-D conversion to 2,4-DCP has been demonstrated in sunflowers, corn, barley, strawberries, and kidney beans. Steen, et al. (1974) found that 2,4-DCP residues in plants treated with 2,4-D herbicide were from 20 to 100 times lower than residues of 2,4-D. Related studies by Sokolov, et al. (1974) involved application of 2,4-D to rice fields. At harvest, rice grain contained neither 2,4-D nor 2,4-DCP even though 2,4-DCP was present in the rice plant. The 2,4-DCP content in potato tubers treated with 2,4-D amounted to less than 10 percent of the total 2,4-D content.

There is little information on the transfer of 2,4-D or its degradation compounds to food products of animal origin. Mitchell, et al. (1946) provided evidence for the gastrointestinal absorption of 2,4-D in lactating dairy cows and detected the herbicide in blood serum during a 106-day oral dosing study. However, 2,4-D was not detected in the milk. More recently, 2,4-D was not found (0.1 µg/g) in bovine milk following oral doses of 5 and 50 µg of herbicide per gram of feed (Gutenmann, et al., 1963a; Bache, et al., 1964a).

Clark, et al. (1975) studied the tissue distribution of 2,4-DCP in sheep and cattle fed 2,4-D at relatively high concentrations of 300, 1,000, and 2,000 µg/g of feed. Assuming that the daily ration is 3 percent of the body weight, this is equivalent to dosages of 9, 30, and 60 mg/kg body weight respectively. The treated diets were fed for 28 days, and resulting concentrations of 2,4-D and 2,4-DCP in several edible tissues were determined (Table 3). With a detection

limit of 0.05 µg/g, analysis did not detect 2,4-DCP in the fat or muscle of cattle and sheep, even at the highest dose levels. However, the kidney and liver were found to contain large amounts of 2,4-DCP proportional to the dose given. Furthermore, when sheep were withdrawn from 2,4-D for 1 week, measurable amounts of 2,4-DCP were still detected. Based on the limited evidence presented, the liver appeared to retain DCP for longer periods than did the kidney. The data presented do not allow accurate calculation of a depletion rate, nor can the total time period of measurable residues be ascertained.

Sherman, et al. (1972) fed technical grade Nemacide (o-(2,4-dichlorophenyl)-o,o-diethyl phosphorothioate) at 50, 100, 200, and 800 µg/g to laying hens for 55 weeks. Analysis for 2,4-DCP (a metabolite of Nemacide) by gas-liquid chromatography (detection limit 0.006 to 0.208 µg/g) resulted in detection of 2,4-DCP residues in liver and yolk, but not in muscle or fat. Details of analytical findings are presented in Table 4. As in the studies of Clark, et al. (1975) there does appear to be some predilection of 2,4-DCP for liver, even when formed by biotransformation from two parent compounds. In the hens studied, liver concentration decreased as the dosage of Nemacide was decreased. The highest mean liver level of 2,4-DCP found in hens was 0.56 µg/g, identical to a mean level of 0.56 µg/g found in the kidneys of cattle fed 9 µg 2,4-D/gm of feed (the dosage level that most closely approximates possible field exposure;

TABLE 3

2,4-D and 2,4-DCP Residues (in mg/kg) in Sheep and Cattle Fed 2,4-D[a]

	2,4-D (Dose mg/kg body weight/day)				
	Sheep		Cattle		
Compound	60	60[b]	9	30	60
			Muscle		
2,4-D	0.06	<0.05	<0.05	<0.05	0.07
2,4-DCP	<0.05	<0.05	<0.05	<0.05	<0.05
			Fat		
2,4-D	0.10	0.15	0.13	0.45	0.34
2,4-DCP	<0.05	<0.05	<0.05	0.05	<0.05
			Liver		
2,4-D	0.98	0.29	<0.05	0.14	0.23
2,4-DCP	0.16	0.15	0.11	0.59	0.31
			Kidney		
2,4-D	9.17	0.37	2.53	8.67	10.9
2,4-DCP	0.26	0.07	0.56	1.17	1.06

[a]Modified from Clark, et al. (1975)

[b]Dosed 28 days, then withdrawn from 2,4-D for 7 days

TABLE 4

2,4-Dichlorophenol Residues in Laying Hens Fed Nemacide (o-(2,4-dichlorophenol)-o,o-diethyl phosphorothioate)[a]

Nemacide feed concentration in ppm	Time since withdrawal from Nemacide	Residues of 2,4-DCP (ppm) mean (and range)	
		Liver	Egg Yolk
800	0	0.47(0.14-0.68)	0.61(0.34-0.75)
	5	- - -	0.27
	7	0.50(0.25-0.75)	
	10	- - -	< 0.122
	14	0.27(0.06-0.48)	
	21	0.19(0.11-0.27)	
200	0	0.38(031-0.44)	0.15(0.12-0.17)
	7	0.30(0.24-0.35)	
	14	0.14(0.09-0.18)	
	21	0.36(0.07-0.64)	
100	0	0.26(0.25-0.26)	0.15(0.12-0.21)
	7	0.56	
	14	0.15(0.0 -0.33)	
	21	0.05	
50	0	0.31(0.16-0.46)	< 0.122
	7	0.18(0.14-0.22)	
	14	0.06(0.05-0.11)	
	21	0.05	

[a]Modified from Sherman, et al. (1972)

see following discussion). Thus, consumption of chicken liver and cattle kidney could result in approximately equivalent human exposure.

Bjerke, et al. (1972) dosed dairy cows with 2,4-D as high as 1,000 mg/kg of diet for 3 weeks. 2,4-DCP was not found in milk or cream of treated cows.

The results of Clark, et al. (1975) can be used to calculate a worst-case estimate for the degree of human exposure to 2,4-DCP from consumption of contaminated meat. Assuming (1) an average forage yield of 2 tons (1,818 kg) per acre, (2) the retention of all herbicide on the treated plants, (3) an application rate of 1 lb (455 gms) of 2,4-D per acre, and (4) consumption by an animal of 3 percent of its body weight in forage, then the dosage delivered to an animal eating forage contaminated with this level of 2,4-D would be approximately 7 mg/kg body weight of 2,4-DCP. This amount corresponds roughly to the lowest dosage (9 mg/kg body weight) that was administered to cattle and sheep by Clarke, et al. Based on the results of Clarke, et al., it is reasonable to expect that cattle fed a constant diet of forage contaminated with 2,4-D applied at commercial rates would accumulate DCP concentrations of approximately 0.11 ug per gram of liver and 0.56 µg per gram of kidney.

If a 70 kg person consumed 0.5 kg of kidney daily at a 2,4-DCP residue concentration of 560 µg/kg, that person would be consuming approximately 280 ug of 2,4-DCP, 0.004 mg/kg body weight daily. If that person also ingested 0.036

mg/kg body weight/day of 2,4-DCP in contaminated drinking water as calculated from 2,4-DCP levels in water downstream from a 2,4-DCP manufacturing plant (see "Ingestion from Water" section), the resultant daily 2,4-DCP dosages would total 0.04 mg/kg. It is clear that the water would contribute 90 percent of this highest calculated daily dosage of 2,4-DCP.

It should be emphasized that an exposure level of 4 ug 2,4-DCP/kg body weight/day is a worst case example for food intake. It would only occur if a person (1) ate 0.5 kg of kidney per day and (2) all the kidney consumed was contaminated with 0.11 μg/g of 2,4-DCP. This contamination level would probably occur only if the cattle were fed a constant diet of 2,4-D-sprayed forage, since experimental evidence (Clark, et al. 1975; Zielinski and Fishbein, 1967) indicates that levels of 2,4-DCP in animal tissue diminished rapidly following withdrawal of 2,4-D from the diet.

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/da. From the data on the 19 major

species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Average Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

No measured steady-state bioconcentration factor (BCF) is available for 2,4-dichlorophenol, but the equation "Log BCF = 0.76 Log P - 0.23" can be used (Veith, et al. Manuscript) to estimated the BCF for aquatic organisms that contain about 8 percent lipids from the octanol/water partition coefficient (P). Based on an octanol/water partition coefficient of 1,200, the steady-state bioconcentration factor for 2,4-dichlorophenol is estimated to be 129. An adjustment factor of 2.3/8.0 = 0.2875 can be used to adjust the estimated BCF from the 8.0 percent lipids on which the equation is based to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for 2,4-dichlorophenol and the edible

portion of all aquatic organisms consumed by Americans is calculated to be 129 x 0.2875 = 37.

Inhalation

There is no direct evidence to indicate that humans are exposed to significant amounts of 2,4-DCP through inhalation. Although the compound is volatile (Table 1), no quantitative studies of inhalation exposure or general environmental contamination have been found.

Dermal

Dermal exposure to 2,4-DCP would most likely occur during the manufacture, transport, or handling of the compound. Due to its lipophilic nature and low degree of ionization at physiologic pH, absorption of 2,4-DCP would be expected; however, no data relating to dermal absorption have been found.

PHARMACOKINETICS

Absorption

No information concerning the direct absorption of 2,4-DCP in humans or animals was found. Toxicity data to be developed later confirm the existence of systemic toxicosis, indicating that 2,4-DCP is absorbed by several routes.

Because of their high lipid solubility and low ionization at physiological pH (Table 1), dichlorophenols would be expected to be readily absorbed via oral intake.

Distribution

No information was found concerning distribution of 2,4-DCP in man. The previously discussed (see "Ingestion from Food" section) animal studies (Clark, et al. 1975;

Sherman, et al. 1972) demonstrated liver, kidney, and egg distribution (see Tables 4 and 5).

TABLE 5

Urinary 2,4-DCP Metabolites of Benzene Hexachloride in Mice[a]

	Form of 2,4-DCP		
BHC Isomer	Glucuronide	Sulfate	Total
gamma-BHC	4-5%[b]	1%	4-6%
beta-BHC	1-2%	3%	4-5%

[a]From Kurihara (1975)
[b]Percent of total metabolites

Metabolism

The biotransformation of 2,4-DCP in humans has not been reported. No information could be found concerning the metabolism of 2,4-DCP administered directly to experimental animals. However, a limited amount of information on the metabolism of 2,4-DCP derived from administration of gamma and beta benzene hexachloride (BHC) to mice was reported by Kurihara (1975). Mice were given C^{14}-labeled gamma- or beta-BHC by intraperitoneal injection, and the appearance of metabolites in urine was monitored. 2,4-DCP and 2,4-DCP conjugates were found and identified primarily as glucuronides and sulfates (Table 6). Administration of gamma-BHC resulted in a majority of 2,4-DCP being conjugated as the glucuronide, while beta-BHC administration resulted in a greater amount of sulfate conjugate. Assuming

that the mouse biotransforms 2,4-DCP resulting from endogenous metabolism in a manner similar to 2,4-DCP directly administered, then sulfate and glucuronide conjugation appear to be major metabolic pathways.

TABLE 6

Acute Mammalian Toxicity of 2,4-DCP

Species	Route of Administration	LD_{50} (mg/kg)	Reference
Rat	Oral	580	Deichmann, 1943
Rat	Subcutaneous	1730	Deichmann, 1943
Rat	Intraperitoneal	430	Farquharson, et al. 1958
Rat	Oral	4000	Kobayashi, et al. 1972
Mouse	Oral	1600	Kobayashi, et al. 1972

Excretion

2,4-D has been found to be rapidly excreted in the urine of mice (Zielinski and Fishbein, 1967), rats (Khanna and Fang, 1966), sheep (Clark, et al. 1964) and swine (Erne, 1966) under various dosing conditions. The phenoxy herbicide MCPA was also rapidly excreted in cattle urine (Bache, et al. 1964b). However, excretion data from studies using 2,4-DCP are not extensive, and no information was found for 2,4-DCP excretion in man.

Karapally, et al. (1973) found that when rabbits were given radioactive gamma-BHC, 2.5 percent of total radioactivity in the urine was due to 2,4-DCP. Data presented did not allow for determination of body burden or half-life. Shafik, et al. (1973) administered a daily dose of Nemacide

in peanut oil orally to rats for 3 days. After administration of 1.6 mg Nemacide, 67 percent of that compound appeared in urine as 2,4-DCP within 3 days. With a dosage of 0.16 mg Nemacide, 70 percent of the pesticide appeared as 2,4-DCP within 24 hours. Work cited earlier (Kurihara, 1975) indicated the appearance of metabolites of 2,4-DCP in urine as a result of gamma- and beta-BHC administration (Table 6).

EFFECTS

Acute, Subacute, and Chronic Toxicity

The mechanism of toxic action for 2,4-DCP in mammalian systems *in vivo* has not been well defined. Limited *in vitro* studies indicate two potential actions. 2,4-DCP inhibits oxidative phosphorylation in rat liver mitochondria and rat brain homogenates (Farquharson, et al. 1958; Mitsuda, et al. 1963). According to Mitsuda, et al. (1963), inhibitory activity of chlorophenols was roughly correlated with the dissociation constant of the inhibitor. In addition, chlorine atoms on the ortho position weakened the activity of mono- and dichlorophenols as oxidative inhibitors. A concentration of 4.2×10^{-5} M of 2,4-DCP inhibited oxidative phosphorylation by 50 percent in rat liver mitochondria. By comparison pentachlorophenol was approximately 40 times more active and dinitrophenol was twice as active in inhibiting oxidative phosphorylation.

Farquharson, et al. (1958) indicated that toxicity of chlorophenols tends to increase when chlorination is increased. Stockdale and Selwyn (1971) showed inhibition of lactate dehydrogenase and hexokinase *in vitro*. Evidence for this effect *in vivo* has not been found and presumably has not been studied.

Farquharson, et al. (1958) offered the conclusion that chlorophenols with pK values of 7.85 or less appear to be acutely associated with production of marked hypotonia, an increase in body temperature, and early onset of rigor mortis after death. Similar clinical effects are associated with well known oxidative uncouplers such as 2,4-dinitrophenol or pentachlorophenol. Relatively few studies of the acute or subacute toxicity of 2,4-DCP are reported. The acute LD_{50} values determined by several investigators are presented in Table 6.

In the study by Farquharson, et al. (1958) acute poisoning of rats, following 2,4-DCP injection, appeared to be characterized by onset of hypotonia approximately 3 minutes after dosing. This effect began in the hindlimbs and moved forward until the rats were prostrate. Eye reflexes were weakened and there was no withdrawal from toe pinch. Muscle twitches occurred rarely and could not be evoked by auditory or tactile stimuli. Rectal temperature was only slightly increased. Initially, there was polypnea, followed by bradypnea. Rigor mortis appeared earlier than in control rats.

The oral LD_{50} derived by Deichmann (1943) appears at odds with the findings of Kobayashi, et al. (1972). Deichmann used fuel oil as a solvent which may have enhanced rapid uptake of 2,4-DCP. The vehicle for the Kobayashi studies could not be determined. Nonetheless, from the LD_{50} values, it appears that 2,4-DCP would constitute an acute hazard only following massive exposure.

In a subacute (10-day) study, Kobayashi, et al. (1972) found that all mice survived when 2,4-DCP at 667 mg/kg was given orally. They derived LD_{50} figures for this study which appear similar to those listed for the acute studies (Table 7). In the same study (Kobayashi, et al. 1972), male mice were also fed 2,4-DCP in the diet over a 6-month period. Parameters evaluated included average body weight, food consumption, organ weight, glutamic oxaloacetate transaminase, glutamic pyruvic transaminase, erythrocyte counts, leucocyte counts, and histopathological changes. The estimated dose levels were 45 mg/kg/day, 100 mg/kg/day, and 230 mg/kg/day, corresponding to dietary 2,4-DCP concentrations of 500, 1,000, and 2,000 ug/g. No adverse effects were noted in mice at any dose level except for some microscopic nonspecific liver changes after the maximum dose. These changes included infiltration of round cells and swelling of hepatocytes with some differences in cell size. Two animals were reported to have "dark cells" in the liver. (To the author's knowledge this term is not commonly used in the United States and its meaning is not clear.) Kobayashi, et al. concluded that 100 mg/kg/day is a maximum no effect level in mice.

TABLE 7

Appearance of Skin Tumors in Mice Treated Cutaneously with Phenols following a Cutaneous Dose of 0.3% Dimethyl Benzanthracene (DMBA) in Acetone[a]

Treatments[b]	Time animals examined (Week)	No. of mice (survivors/total)	Survivors with papilloma (%)	Average papillomas per survivor	Survivors with epithelial carcinoma (%)
Benzene control	15	15/20	7	0.07	0
Benzene control	24	27/32	11	0.15	0
10% phenol in benzene no DMBA	20	24/30	33	0.62	13
20% phenol in acetone	12	21/24	58	-	5
20% phenol in benzene	24	10/33	100	3.20	20
20% 2,4-DCP in benzene	15	27/33	48	1.07	11
20% 2,4-DCP in benzene	24	16/23	75	1.62	6

[a] Source: Modified from Boutwell and Bosch (1959)
[b] All received DMBA except where stated

No other chronic toxicity studies using 2,4-DCP have been found. One report in the literature (Bleiberg, 1964) has suggested a possible role of 2,4-DCP in acquired chloracne and porphyria in workers manufacturing 2,4-DCP and 2,4,5-trichlorophenol (2,4,5-TCP). The workers involved were also exposed to acetic acid, phenol, monochloroacetic acid and sodium hydroxide. Since various dioxins (including 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD) which has been associated with chloracne) have been implicated as contaminants of 2,4,5-TCP, the role of 2,4-DCP in inducing chloracne and porphyria is not conclusive (Huff and Wassom, 1974).

Synergism and/or Antagonism

Reports of studies directly assessing the synergism or antagonism of 2,4-DCP by other compounds were not found. Since 2,4-DCP is an oxidative uncoupler (Mitsuda, et al. 1963), it may be expected that concomitant exposure to other uncouplers (e.g., pentachlorophenol, dinitrophenol) would enhance that effect. In addition, exposure to gamma- or beta-BHC, 2,4-D, and nitrofen could add slightly to any primary body burden of 2,4-DCP.

Any agent causing liver damage sufficient to decrease the conjugation of 2,4-DCP with glucuronide or sulfate could conceivably alter the excretion and/or toxicity of the parent compound. However, there are no specific studies to reflect such an effect.

Teratogenicity

No studies were found which addressed the teratogenicity of 2,4-DCP.

Mutagenicity

No studies were found which addressed the mutagenicity of 2,4-DCP in mammalian systems. Amer and Ali (1968, 1969) did report some effects of 2,4-DCP on mitosis and meiosis in flower buds and root cells of vetch (Vicia faba). Changes included meiotic alterations of chromosome stickiness, lagging chromosomes, and anaphase bridges when flower buds were sprayed with 0.1 M 2,4-DCP. Mitotic changes of chromosome stickiness, lagging chromosomes, disintegration, bridging, disturbed prophase and metaphase, and occasional cytomyxis were seen in root cells exposed to 62.5 mg/l DCP. Later studies (Amer and Ali, 1974) further confirmed the effect of chromosome stickiness, lagging chromosomes, and fragmentation in 35-day-old Vicia faba. The relationship of these changes to alterations in mammalian cells has not been established.

Carcinogenicity

Repeated application of phenol and some substituted phenols has demonstrated promoting as well as complete tumorigenic activity (Boutwell and Bosch, 1959). In this study, two trials included evaluation of 2,4-DCP as a promoter. In one trial 2 ul of a 20 percent solution of 2,4-DCP in benzene was applied twice weekly for 15 weeks to female Sutter mice 2 to 3 months of age. The other trial was identical except that 2,4-DCP was applied for 24 weeks. Application in both trials followed an initiating dose of 0.3 percent dimethyl-benzanthracene in benzene.

The 2,4-DCP dose used corresponds to 5 mg of compound per mouse at each application, or 10 mg/week when applied

twice weekly. Sutter mice 2 to 3 months old would be expected to weigh 35 grams, so that the dose rate would be 40.82 mg/kg body weight.

Tumorigenic response was measured as follows:

1) The percentage of surviving mice bearing one or more papilloma was ascertained.
2) The number of papillomas on <u>all</u> surviving mice was totaled and divided by the number of survivors to give the average number of papillomas per mouse.
3) The number of mice bearing malignant tumors was determined.

Results of the promoter trial with 2,4-DCP are presented in Table 7. Related promoter experiments with phenol and the two benzene controls are included for comparative purposes. Boutwell and Bosch concluded that the promoting activity of 2,4-DCP is similar to that of phenol. However, no statistical analyses nor dose-response data were included to support this comparison.

To see if there was a statistically significant difference between the 2,4-DCP-treated mice and the benzene controls, a Fisher exact test was undertaken for this document. Tumor incidence was derived with the assumption that only survivors were examined for tumors. The calculated results are presented in Table 8.

TABLE 8

Results of Fisher Exact Test Applied to Data from Boutwell and Bosch (1959)

Treatment	Duration of treatment (wks)	Incidence of papillomas	P-value vs. control	Incidence of epithelial carcinoma	P-value vs. control
benzene control (I)	15	1/15	-	0/15	-
20% 2,4-DCP in benzene	15	13/27	0.61×10^{-2}	3/27	0.2548
benzene control (II)	24	3/27	-	0/27	-
20% 2,4-DCP in benzene	24	12/16	0.36×10^{-4}	1/16	0.3721

This analysis indicates that (1) the higher incidence of papillomas in both 2,4-DCP-treated groups was not attributable to chance, and (2) the carcinoma incidence was not significantly elevated over controls.

This statistical exercise should not obscure a number of considerations that could affect the meaningfulness of the results. (1) The study used dermal application of a phenolic compound at 20 percent concentration in organic solvents. This concentration is high enough to destroy hair follicles and sebaceous glands. The papillomatous response observed may have developed in response to chemical and/or physical damage from application of an irritant compound. (2) Even with the harsh treatment, no malignant neoplasia was observed except when DMBA was used as an initiator. The only neoplasia observed was at the site of direct appli-

cation. (3) Pathological identification of benign and malignant tumors was done on a gross level, with only periodic confirmation by microscopic examination.

The report of Boutwell and Bosch (1959) is the only one found that deals with the tumorigenicity of 2,4-DCP. However, since the study was designed primarily to detect promoting activity, the effect of 2,4-DCP as a primary carcinogen is not well defined.

The route of administration is not appropriate to the model for carcinogenic risk assessment and has no established relationship to oral exposure. Overall, the study does present evidence that 2,4-DCP may be a possible promotor, and the work may be applicable to evaluating the hazard of skin or respiratory exposure to 2,4-DCP, alone or concurrent with other chemicals.

Other Effects

An odor threshold for 2,4-DCP in water has been reported by at least two investigators. Hoak (1957) determined the odor threshold of 2,4-DCP to be 0.65 µg/l at 30°C and 6.5 µg/l at 60°C. Determination of the detectable odor was made by a panel of two to four people comparing flasks of test water to a flask of odor-free water. The lowest concentration detected by any panel member was taken as the odor threshold. Hoak speculated that odor should become more noticeable as temperature increases; however, in evaluating a series of chlorophenols and cresols, it was found that some compounds had higher odor thresholds at 30°C and others were higher at 60°C. Burtschell, et al. (1959) made

dilutions of chlorophenol in carbon-filtered tap water and used a panel of four to six people to evaluate odor. Tests were carried out at room temperature which the investigator estimated to be 25°C. If a panel member's response was doubtful, the sample was considered negative. The geometric mean of the panel responses was used as the odor threshold. For 2,4-DCP the threshold was 2 µg/l. The data presented do not indicate a range of responses, but because of the variability inherent in such procedures, it seems reasonable that the odor threshold for some evaluators in the Burtschell group would extend downward toward the 0.65 µg/l figure of Hoak.

CRITERION FORMULATION

Existing Guidelines and Standards

Presently no standard for exposure to 2,4-DCP in drinking or ambient water has been set (Natl. Acad. Sci., 1977), although a standard of 0.1 mg/l for 2,4-D, a related compound, has been set (Natl. Acad. Sci., 1977).

Current Levels of Exposure

Human exposure to 2,4-DCP has not been monitored, but a worst-case estimate of 0.04 mg 2,4-DCP/kg body weight/day of exposure was presented in the "Ingestion from Food" section.

Special Groups at Risk

The only group expected to be at risk for high exposure to 2,4-DCP is industrial workers involved in the manufacturing or handling of 2,4-DCP and 2,4-D. No data were found to relate exposure or body burden to conditions of contact with 2,4-DCP.

Basis and Derivation of Criterion

Insufficient data exist to indicate that 2,4-DCP is a carcinogenic agent. The only study performed (Boutwell and Bosch, 1959) was designed to detect promoting activity, and the effect of 2,4-DCP as a primary carcinogen could not be evaluated. Also, the route of administration in this study (dermal) is inappropriate for use in the linear model for carcinogenic risk assessment (see "Carcinogenicity" section). In fact, only minimal health effects data exist on the acute and chronic effects of 2,4-DCP. Only one study of a chronic nature (Kobayashi, et al. 1972)

was found. They determined a chronic (6-month) no-effect level for 2,4-DCP of 1000 µg/g of diet for mice, which is equivalent to 100 mg/kg body weight per day. For water, a concentration of approximately one-half the dietary intake will result in equivalent dosage on a body weight basis, assuming a fluid intake two times the dry matter intake.

If food sources are not included, the maximum no-effect level of 2,4-DCP in water for mice would be 500 µg/ml. Applying an uncertainty factor of 10^{-3} X maximum no-effect level as suggested by the National Academy of Sciences Safe Drinking Water Committee (Natl. Acad. Sci., 1977) would result in a criterion for human health of 500 µg/liter, which is approximately 250 times greater than the threshold odor concentration reported by Burtschell, et al. (1959).

However, in addition to exposure through drinking water, additional exposure to 2,4-DCP through the daily ingestion of 18.7 g of fish and shellfish products exists. Therefore, based on the assumption of an intake of 2 l of drinking water per day at a level of 500 µg/l, and a fish bioconcentrating value of 37, the total amount of 2,4-DCP exposure through both routes is 371 µg/day:

$$\frac{2 \times 500 \text{ µg/day}}{2 + (37 \times 0.0187)} = 371 \text{ µg/day}$$

Human health is a subjective measurement in many respects. The organoleptic effects of 2,4-DCP could conceivably alter human health by causing a decrease in water consumption. This might be of particular importance to individuals with certain renal diseases or in instances where

dehydration occurs as a result of vigorous exercise, manual labor, or hot weather. Although two investigators reported that low concentrations of 2,4-DCP caused discernible odor, neither indicated if the threshold odor concentration made water unacceptable for consumption. In view of the wide disparity between odor threshold concentrations and available toxicity information, the criterion recommended is based on organoleptic effects. It is suggested that a 2,4-DCP water concentration of 0.5 µg/l would be low enough to prevent objectionable organoleptic effects for most people and still be far below minimal no-effect concentrations determined in laboratory animals.

In conclusion, two criteria can be proposed. Based on the prevention of adverse organoleptic effects, the interim criterion recommended for 2,4-dichlorophenol is 0.5 ug/l in water. Based on human health effects alone, the interim criterion recommended is 371 µg/l.

It should be emphasized that data are needed in the following areas to properly evaluate any hazard from 2,4-DCP:

1) Monitoring of worker exposure to 2,4-DCP in industries manufacturing or using the chemical.
2) Monitoring of public water supplies and industrial and municipal effluents to determine an expected range of concentrations under differing environmental conditions.
3) More definitive studies of residue kinetics of 2,4-DCP in food animals which are exposed to products capable of generating 2,4-DCP.

4) Evaluation of chronic toxicity, mutagenicity, and teratogenicity of 2,4-DCP using currently acceptable techniques.

5) A carcinogenicity study of 2,4-DCP using the oral route and evaluated according to current protocols.

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